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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,523	10/24/2003	Nicholas G. Bacopoulos	24852-501 CIP4	9840

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EXAMINER	
DELACROIX MUIRHEI, CYBILLE	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,523	BACOPOULOS ET AL.	
	Examiner	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-94 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-94 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claims 1-94 are presented for prosecution on the merits.

Information Disclosure Statement(s)

Applicant's information disclosure statements received April 6, 2004, March 14, 2005 and June 9, 2005 have been considered. Please refer to applicant's copies of the 1449 submitted herewith.

Claim Rejection(s)—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-65, 69-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiMartino, 6,905,669.

DiMartino discloses methods of treating cancer by administering to a patient in need thereof an effective amount of a pharmaceutical composition containing a DNA methylation inhibitor and a histone deacetylase inhibitor (HDAC). Specifically, examples of HDAC inhibitors that may be used in the cancer treatment methods are SAHA, (claims 1, 27, 35, 43, 50, 57) and pyroxamide (claim 65). Examples of cancers include hairy cell tumor, acute and chronic lymphocytic tumors, acute myeloid leukemia, chronic myelogenous leukemia, acute promyelocytic leukemia, acute lymphoblastic leukemia (col. 17, lines 35-67; col. 18, lines 1-26)). The HDAC inhibitors may be administered orally, parenterally or may be administered in slow release formulations (col. 20, lines 56-59; col. 21, lines 7-8). Finally, DiMartino discloses that other HDAC inhibitors may be administered such as trichostatin A or CBHA (col. 5, lines 39-54). Please also see col. 9, lines 12-27; col. 13, lines 58-62

DiMartino does not specifically disclose that the HDAC inhibitors, alone, i.e. when not combined with the DNA methylation inhibitor, may be administered to treat the above-described leukemias. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat cancer such as leukemia with the disclosed HDAC inhibitors because, DiMartino suggests that, individually, the HDAC inhibitors demonstrate anti-cancer or anti-leukemia, and one of ordinary skill in the art would reasonably expect the HDAC inhibitors, by themselves, to be therapeutically effective against leukemia.

Also, please note that applicant's claims recite "comprising" language. According to MPEP 2111.03, "[t]he transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.");< Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Thus, since the pending claims are open-ended due to the use of "comprising" language, they do not exclude the additional DNA methylation inhibitors taught by DiMartino.

DiMartino does not specifically disclose applicant's claimed dosage amounts and timing

of administration. However, since therapeutic efficacy is related to the amount (dosage) of active agent administered as well as timing of administration, it would have been obvious to one of ordinary skill in the art to further modify the methods of DiMartino such that the HDAC inhibitors administered in an amount and for a period of time effective to optimize treatment of the various forms of leukemia.

Finally, concerning the specifically claimed pharmaceutical excipients and capsule formulations, these are art-recognized result-effective variables and it would have been obvious to one of ordinary skill in the art to optimize them in the methods of DiMartino.

2. Claims 66-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiMartino as applied to claims 1-65 and 69-94 above, and further in view of WO 98/55449 ('449) and WO 95/31977 ('977).

DiMartino as applied above.

DiMartino does not disclose treating leukemia by administering to a patient in need thereof a composition comprising the compounds of claims 66-68. However, the examiner refers to WO '449, which discloses a method of treating a variety of tumor cell types by administering an effective amount of a composition containing a compound of Formula (Ia). WO '449 teaches that the compounds are capable of inhibiting deacetylation of histones (abstract; page 6). Furthermore, the compounds may be used to treat cancers such as leukemia and lymphomas (pages 7, 19).

The examiner also refers to WO '977, which discloses a method of treating cancer by administering to a patient in need thereof an effective amount of a composition containing a compound as described at page 12, lines 25-35. The compound is capable of inhibiting the proliferation of neoplastic cells, and WO '977 additionally discloses that cancers such as acute leukemia may be treated by administration of the disclosed compound (page 30).

Therefore it would have been obvious to one of ordinary skill in the art to further modify the methods of DiMartino by administering to the leukemia patients of DiMartino the compounds taught by WO '977 and '449 because, in view of the desirable anti-leukemia activity and histone deacetylase inhibiting activity taught by WO '977 and '449 one of ordinary skill in the art would reasonably expect the compounds of WO '449 and '977 to be equally effective in inhibiting the proliferation of leukemia cells in the patient taught by DiMartino.

Conclusion

Claims 1-94 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
Sep. 19, 2005

Cybille Delacroix-Muirheid
Patent Examiner Group 1600